

Independent evidence-based health care

All our yesterdays

"..have lighted fools the way to dusty death". That was one Scottish king's take on the past, according to our Will. Put that with the knowledge that a lie will go round the world while the truth is pulling its boots on, and you get a flavour of this 10th anniversary issue of **Bandolier**.

We visit myths and legends: those things stated with conviction, but for which there is little fact, or where facts tell us otherwise. **Bandolier** is remiss in not doing more about myths and legends. Perhaps we concentrate too much on evidence, instead of scotching and killing snakes of myths and legends.



This month, then, we start a mythbuster series with two examples. One is that ibuprofen does not work in women. A second is the suggestion that heart attacks and strokes are more severe in people who take statins than in those who do not. Neither has a vestige of truth in them, and for both there is a superabundance of evidence that they are false myths. We also review a book about statistics and statisticians by Stephen Senn, a man not to be trifled with as he can name six famous Belgians. For 2004, we invite readers to send us examples of myths and legends for some evidential mythbusting.

Other stuff

The first issue of **Bandolier** looked at GRiP, getting research into practice. Again, an important topic on which we (and others, for that matter) should do more. A heartening tale comes from the Veterans healthcare system in the USA, where a way was found to get an organisation to put evidence into practice, with great results. Why don't people write about how they managed to make a difference? **Bandolier** has room on its Internet site for those who would like to help others do what they have done.

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MANAGING TO MAKE A DIFFERENCE

Ten years ago the very first issue of **Bandolier** concerned itself with the topic of getting research into practice, or GRiP. Getting a grip on management and quality of healthcare services has become a core issue for many health services since then. The trouble is that quality is an awfully difficult thing to measure, and outcomes are hardly ever affected by a single technology. Most of what we do is to use complex packages of care with many technologies.

Things do get better, though. **Bandolier** 82, for instance, showed how handwashing practice in a Geneva hospital was improved to reduce hospital acquired infection. **Bandolier** 100 examined improvements in treatment after heart attacks in South Derbyshire. But there are few reports about system-wide changes that make a difference. Now we have one [1] from the Veterans Affairs administration in the USA that shows that major changes can make major differences.

Background and intervention

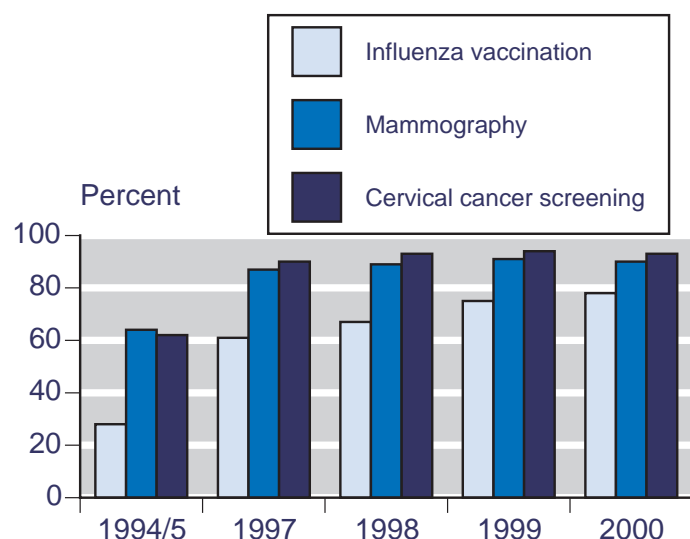
After criticism of the service in the early-mid 1990s, the VA launched a major re-engineering of its health care system, aiming to use better information technology, measurement and reporting of performance, integration of services and realigned payment policies. The years 1994 and 1995 were used as baselines, and the present study [1] examined a number of quality of care markers over succeeding years to investigate how the re-engineering made a difference. It also examined comparable national data from the Medicare programme.

Indicators chosen were of various sorts. In preventive medicine they included cancer screening and vaccination. Out-patient care was examined looking at diabetes care, for instance, with annual eye examinations and glycosylated haemoglobin (HbA1c) measurements. For inpatient care indicators included aspirin immediately after heart attack and at discharge, and smoking cessation counselling in hospital. In all 17 indicators were used.

Results

About 48,000 patients were included in the baseline years, with more patients in subsequent years. Performance for 13 indicators where information was available for all years rose substantially, with statistically highly significant improvements in 12 of them. Examples for influenza vaccination and screening for breast and cervical cancer are shown

Figure 1: Changes in VA healthcare - 1



in Figure 1, and for outpatient diabetes and aspirin on discharge after a heart attack in Figure 2.

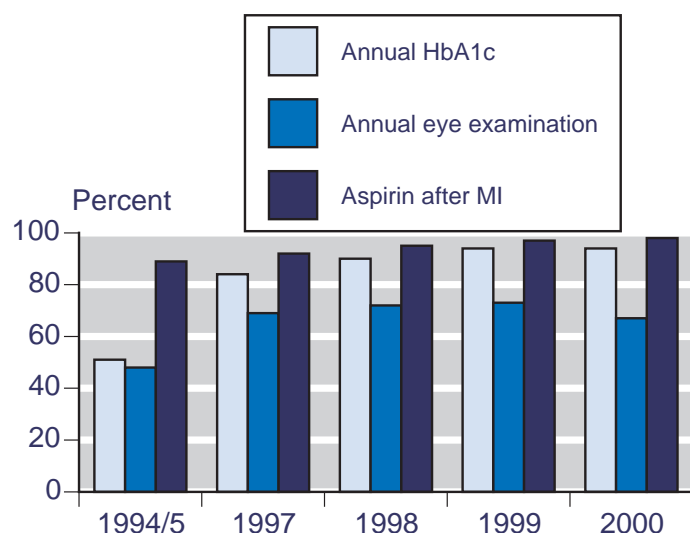
For 11 indicators, comparison was possible with Medicare in the years 1997-1999 and 2000-2001. In each case quality performance was higher in the VA than Medicare, sometimes substantially so.

Comment

Of course there are all sorts of limitations with this sort of retrospective study. It could have been that there was a general change in US healthcare, and that the VA improvement simply mirrored this change. The comparison with Medicare implies that this was not the case. There may have been sampling differences, or age structure differences, though this was unlikely. And perhaps the indicators chosen just happened to be easy targets.

The most likely reason for the change was the operational reorganisation and implementation of quality management principles inside the VA. In this, performance contracts held managers accountable for meeting improvement targets, with data gathering and monitoring performed by an independent agency, and made public. This was made possible

Figure 2: Changes in VA healthcare - 2



by instituting an integrated, comprehensive electronic medical records system. Not mentioned were league tables, star ratings, sackings, or direct political oversight, though apparently members of Congress kept a beady eye on progress.

There are lessons here. The most important is the knowledge that it is possible to make big changes in complex healthcare systems in a relatively short time and in a number of areas at the same time. Interestingly, the authors report that the budget of the VA was “essentially flat” between 1995 and 2000, while the number of patients increased by 40%. Food for thought for us all, and the hope that at least one organisation has seen gain. What was not reported was the amount of pain inside the organisation to achieve it.

Reference:

- 1 AK Jha et al. Effect of the transformation of the Veterans Affairs health care system on the quality of care. *New England Journal of Medicine* 2003 348: 2218-2227.

NSAIDs FOR PRIMARY DYSMENORRHOEA

What extra can we find out about a topic when another systematic review comes along, as a Cochrane review [1] on NSAIDs for dysmenorrhoea? A previous review showed specific NSAIDs to be effective [2], but this newer review of NSAIDs takes a very critical view.

Systematic review

The Cochrane Menstrual Disorders and Sub-fertility Group trials register, Cochrane Central Controlled Trials Register, MEDLINE, and EMBASE were searched for randomised double blind trials of NSAIDs in primary dysmenorrhoea. Active and placebo controlled trials were included. Outcomes analysed were pain relief, absence from work or school, restriction of daily activities, and adverse effects. Studies in which fewer than 80% of randomised patients were available for a particular outcome were excluded.

Results

Sixty-three randomised controlled trials with 4,006 women were included, of which 44 used a crossover design. All were described as double-blind and eleven had adequate allocation of concealment. Information from crossover designs was used only if dichotomous data on the first treatment phase was available. Fourteen placebo-controlled trials had information on pain relief, and were all very small, with treatment group sizes between 15 and 35 women.

Women were aged between 12-47 years. Doses of NSAIDs varied across trials but were within the recommended daily doses. The duration of treatment was generally 3-5 days. Few trials compared the same treatments so there was sparse information available for any particular NSAID and most analyses were based on results from a single study. Findings of the meta-analysis were supported by direct comparisons of different NSAIDs, and crossover trials.

Efficacy

Most information was available for pain relief. Of 36 trials comparing NSAIDs with placebo, 14 (599 women) reported the number of women with at least moderate pain relief and were included in the meta-analysis. Results varied widely across trials (Figures 1 and 2) with between 5-40% (mean 20%) of patients achieving at least moderate pain relief with placebo and 17-95% (mean 67%) with NSAIDs. Overall there was a significant benefit with NSAIDs compared with placebo, relative benefit 3.4 (2.5 to 5.4) and NNT 2.1 (1.9 to 2.5) for at least moderate pain relief over 3-5 days. Most information was for naproxen (Figure 1) with an NNT of 2.5 (2.0 to 3.3). Figure 2 shows results by particular NSAIDs, including some cross-over trial data.

Requirement for additional medication and absence from work or school were reported less often. Women taking NSAIDs were less restricted in their daily activities than women taking placebo (216 women, 39 % restricted vs 68% placebo), and were less likely to be absent from work or school (229 women; 36% versus 72%).

Adverse effects

Overall NSAIDs caused significantly more adverse effects than placebo (1030 women), but there was no significant difference between NSAIDs and placebo for gastrointestinal effects (432 women) or nervous system adverse effects (229 women).

The median withdrawal rate of was 10%. Women withdrew for reasons including lack of efficacy or adverse effects, but numbers for these were not available.

Comment

Despite the inclusion of a large number of trials, they generally had uninterpretable designs, they were small, with

Figure 1 Percent of patients with at least moderate pain relief in placebo controlled trials included in the meta-analysis (naproxen in open circles, other NSAIDs in filled circles)

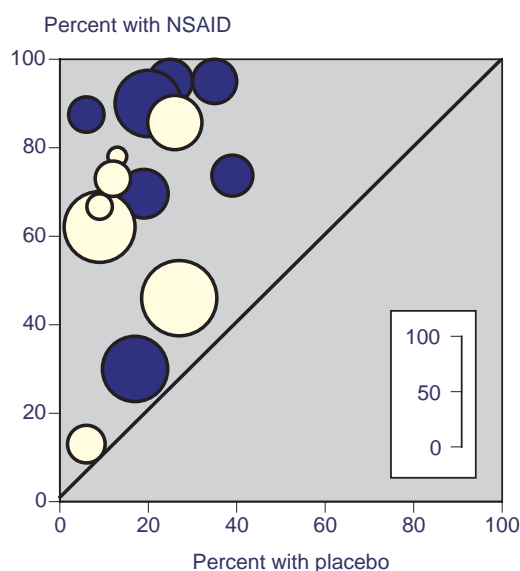
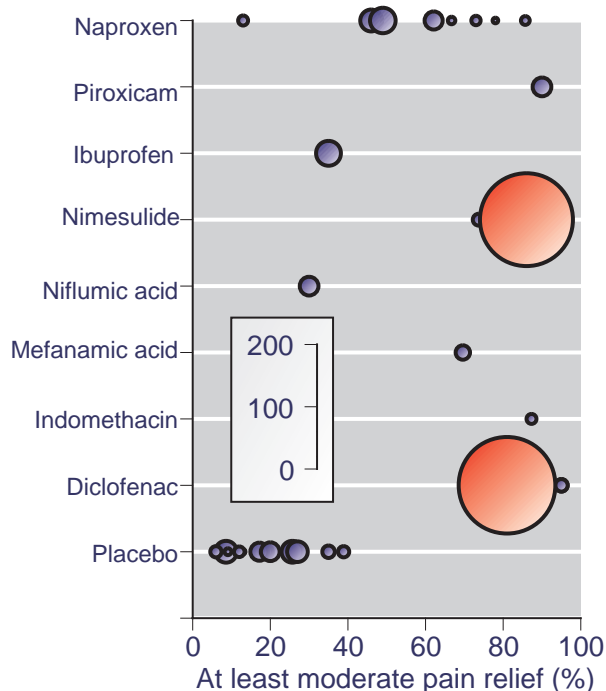


Figure 2 Percent of patients with at least moderate pain relief with particular NSAIDs. All trials included in the meta-analysis



too few patients to make much sense for different NSAIDs. That so many crossover trials failed to report results for the first treatment phase meant that much of the available information could not sensibly be included in the meta-analysis. We know that NSAIDs are effective, but we do not know which dose of which NSAID is the most effective and least harmful. Figure 2 is the closest we can come to a comparison of efficacy, and that is not much help because there is so little data. While pain is a useful outcome, and while reduction in pain suggests a reduction in other things like restriction of activities and absenteeism from work or school, we have no idea what women think is the most important outcome for them. One might have hoped for more information than this.

Frankly, in 2004, this is a disgrace. Half the population are women, dysmenorrhoea affects half of them, and one in 10 is incapacitated by it every month. Yet all we have is information on fewer than 600 women in trivial trials. It is just not good enough.

Reviews all too often moan on about the need for more research in a rather unthinking way, but here is a barn door case for more and better research. We might have some from pharmaceutical companies with new analgesics to sell, but the comprehensive research needed will only come when health services take an interest. **Bandolier's** feminine side is writing to her parliamentary representatives.

References

- 1 J Marjoribanks et al. Nonsteroidal anti-inflammatory drugs for primary dysmenorrhoea (Cochrane Review). In: the Cochrane Library, Issue 4, 2003.
- 2 WY Zhang, A Li Wan Po. Efficacy of minor analgesics in primary dysmenorrhoea: a systematic review. British Journal of Obstetrics & Gynaecology 1998 105:780-789.

MYTHBUSTER:

IBUPROFEN AND WOMEN

Bandolier seems to have spent a lifetime being told things that, on chasing up, were just not true. In the medical world, this can be a reference to a reference to a reference, which, when read, finds that something was tried in two men and a dog, and the dog got better (or died). Or it can even be that a much-quoted reference does not actually exist. These things are irritating beyond belief, but ultimately one has the satisfaction of nailing the myth.

Other myths and legends are much more difficult. They are vague, or seemingly unimportant, or seemingly important but apparently backed up by evidence of a sort (there is evidence that...). **Bandolier** finds that so often this sort of evidence turns out to be a distortion of facts or statistics, but unless the myth or legend immediately sets alarm bells ringing, it gets past the filters and directly into memory. The first Mythbuster is about a myth that immediately set alarm bells ringing and was nailed.

Ibuprofen and women

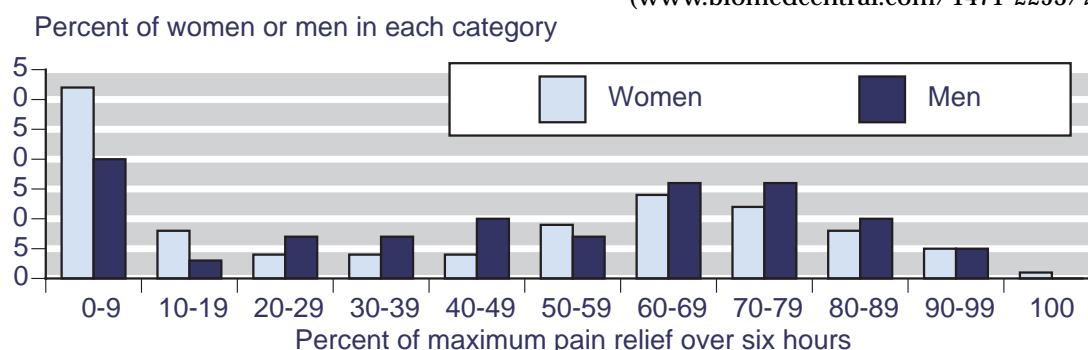
A researcher was told by a chiropractor that ibuprofen was ineffective in women, based on an article in the New Scientist in January 2002 written by a science writer in residence at the Novartis Foundation. A single study of experimental pain in 10 women and 10 men was the source of the assertion that ibuprofen was ineffective in women, supported by the claims that this was clinically important. A further assertion was that women were under-represented in clinical trials of analgesics, which was why clinical trials had failed to show the ineffectiveness of ibuprofen. The researcher just happened to be updating a Cochrane review on ibuprofen, so alarm bells were a bit loud.

Mythbusting

This took the form of:

- 1 Searching for papers relating to ibuprofen in women, especially systematic reviews and meta-analysis.
- 2 Analysing individual patient data for differences in response between men and women.
- 3 Examining randomised trials of ibuprofen in acute pain for the presence of women in the trials.

Figure 1: Pain relief experienced by women and men given 400 mg ibuprofen



Results

Searching showed that there was abundant evidence that ibuprofen did work in women. For example:

- ◆ An FDA individual patient analysis in 300 patients found no gender difference in response rates for ibuprofen after third molar removal.
- ◆ A review of primary dysmenorrhoea reported that pain was effectively treated with ibuprofen.
- ◆ Systematic reviews and scores of randomised trials of ibuprofen and other NSAIDs and coxibs in osteoarthritis and rheumatoid arthritis, in which women predominated, showed good efficacy, with no evidence that ibuprofen did not work in women.

The paper also looked at 37 trials comparing ibuprofen and placebo in acute pain. None had fewer than 45% women. Thirty-two had more than 50% women. Eight trials enrolled only women, and no trial enrolled only men. Individual data from over 300 women and 300 men showed no difference in the range of responses with ibuprofen (Figure 1).

Comment

Ibuprofen works in women, and women have predominated in clinical trials involving it. Recently the myth that it does not work in women has appeared again, and seems continually to be recycled in magazines. This seems to be the way of myths and legends.

How did it start? Selective reporting of data. Picking out a single study that supported a proposition, and then hyping it with other selected quotes and comments, and with an agenda about medicines not being tested in women overlaying it. An argument was built on sand, but believable because of the highly respected journal in which it appeared. And the original study itself was suspect - very small and in experimental pain, which those in the field know bears no relation to clinical work.

Don't forget to give importance to the dogs that didn't bark in the night. Ibuprofen has been around for decades. Does anyone really think that millions of clever-clogs medical professionals might have overlooked the lack of pain relief in half the population that used it?

Reference:

- 1 J Barden et al. Ibuprofen 400 mg is effective in women, and women are well represented in trials. BMC Anaesthesiology 2002; 2:6 (www.biomedcentral.com/1471-2253/2/6)

MYTHBUSTER: STATINS AND EVENT SEVERITY

Myths and legends come in a variety of forms, and sometimes they astound. Faced with an older woman with raised cholesterol and a family history of heart disease, most of us would think of statins as being an important part of risk reduction. How would you then react when she told you that a doctor had informed her that taking statins might reduce the risk of something happening, but that if it did happen she would be left as a “vegetable”? She should choose whether to take a statin, and had chosen not to.

The problem

Now the first problem is that you don’t know what was actually said to her, nor the context in which it was said. And you are not absolutely sure what was meant or how it was meant to be taken, or taken to be meant.

One interpretation is that she has been correctly told that statins reduce the risk of heart attack and stroke, but that should heart attacks or stroke actually occur in people taking a statin, those events would be much more severe. How might we look for evidence that this is a myth or true? Some suggestions:

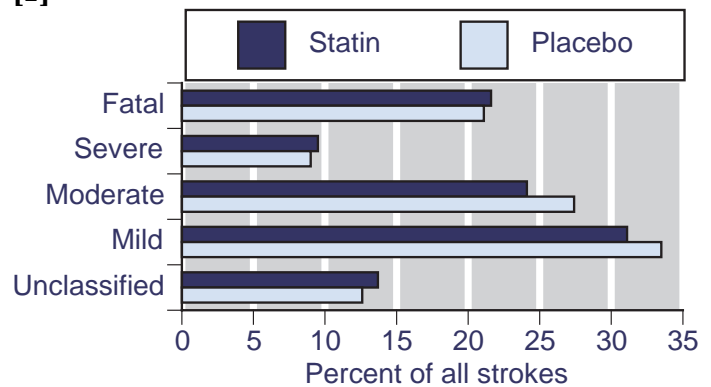
- 1 Do a literature search for statin and event severity, using infarction, stroke, and combinations of words to try to find case reports. The logic here is that doctors are anything but daft, and that in the last 10 years or so, when statin use has become ever more widespread, someone, somewhere, would have noticed an epidemic of severe heart attacks or strokes and made the connection.
- 2 Examine the large randomised statin trials to see whether any have reported on severity of events compared with placebo.
- 3 Look at any other studies with statins that might have been expected to comment on event severity.
- 4 Ask your friends if they have any better ideas.

Results

Bandolier tried all four of these. The results we found were as follows:

- 1 Several hours of searching and reading of abstracts found not a single case report alleging that statin use resulted in more severe outcomes for heart attack or stroke.
- 2 The heart protection study [1] enrolled 20,000 high risk people in a randomised comparison of simvastatin 40 mg daily and placebo for an average of five years. A quarter of them were women, and almost a third over 70 years. There were 444 strokes in those taking statins, and 585 in those taking placebo, a reduction in frequency of 25%. The authors also helpfully reported stroke severity (Figure 1). Severity of strokes that occurred was exactly the same in those on a statin as those on placebo. This is solid evidence that there was no increase in stroke severity with statins.

Figure 1: Stroke severity occurring in statin and placebo users in Heart Protection Study [1]



- 3 A study of events in the 30 days after admission in patients with coronary artery disease and chest pain treated with statins throughout (369 patients) and not having a statin before or after admission (1151 patients) was related in **Bandolier** 113. The events seven days after admission are shown in Figure 2. Not only were there fewer events in total in those who were on a statin, but those that occurred were, if anything, less rather than more severe.
- 4 None of **Bandolier**’s friends who were asked about this had any other knowledge of any evidence that could support the proposition that statin use led to worse outcomes. All were mystified by the suggestion.

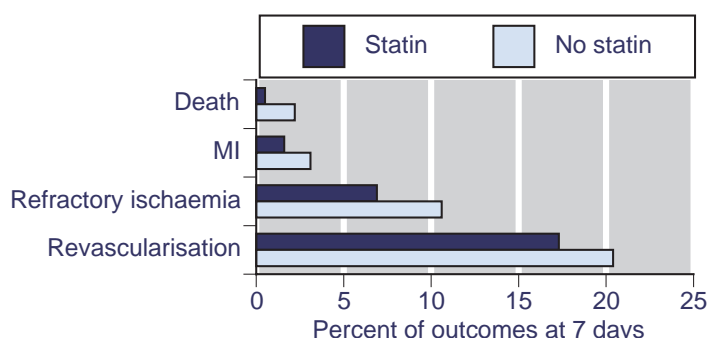
Comment

This is one myth that can confidently be busted. Not only is there the clearest and most abundant evidence that statins reduce the risk of heart attack and stroke in people at almost all levels of risk, but there is also compelling evidence that outcomes are no worse with statins.

References:

- 1 Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20 536 high-risk individuals: a randomised placebo-controlled study. *Lancet* 2002 360: 7-22.
- 2 C Heeschen et al. Withdrawal of statins increases event rates in patients with acute coronary syndromes. *Circulation* 2002 105: 1446-1452.

Figure 2: Outcomes within seven days of admission to hospital with chest pain in statin users and non-nusers [2]



ASPIRIN AND PANCREATIC CANCER

Friday is “health-scare-in-the-media” day. Just recently **Bandolier** was regaled over its low-salt muesli and fruit by a story that use of aspirin caused pancreatic cancer in women. It seemed serious. One experienced presenter was quizzing the (good) media doc about whether women should just stop taking aspirin altogether.

Serious stuff this. So a quick look at the evidence, and a read of the paper [1] suggested that things might not be quite so bad. Actually all the increased risk was in women taking more than 14 aspirin tablets (325 mg equivalents) a week for more than 20 years. And even then the increased risk only just reached statistical significance.

Study

This was part of the Nurses’ Health Study that enrolled 122,000 female nurses in 1976 and has been following them up ever since. Information on aspirin use was first collected at baseline and then regularly thereafter, as well as information about other risk factors. Pancreatic cancer and deaths were included in biennial questionnaires, and confirmed by review of the medical records.

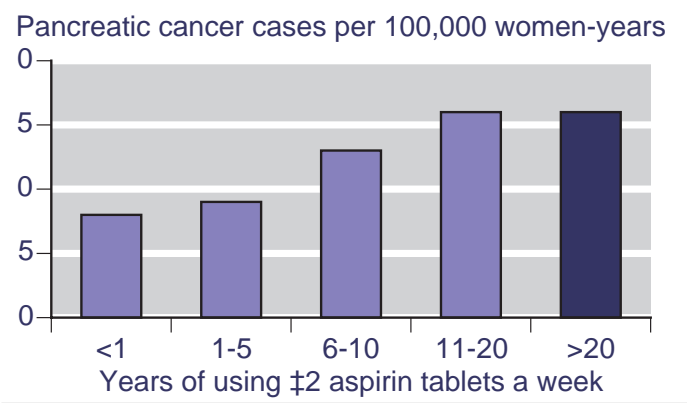
Excluded were nurses who either failed to respond to the baseline questionnaire, did not provide information on aspirin use, or with a baseline history of cancer. There are many details in what was an unquestionably fine study.

Results

Information was available for 88,378 women, who reported 161 cases of pancreatic cancer over 18 years. In women who were not regular users of aspirin there were 96 cases, with a crude rate of 10 cases of pancreatic cancer per 100,000 women years. In women who did use aspirin regularly (more than two 325 mg aspirin tablets a week) there were 65 cases, 13 per 100,000 women years, a non significant increase.

Regular use of aspirin for longer periods was associated with higher rates of pancreatic cancer, but this only became significant in women who used aspirin regularly for more

Figure 1: Pancreatic cancer according to duration of aspirin use (≥2 tablets a week): darkest bar is statistically significant



than 20 years (Figure 1). There were 34 cases in these women, and relative risk adjusted for a number of variables just reached statistical significance, with a relative risk of 1.6, and a 95% confidence interval of 1.03 to 2.4.

Regular use of more aspirin was also associated with higher rates of pancreatic cancer, but this only became significant in women who regularly used more than 14 aspirin tablets a week for at least 6-8 years (Figure 2). There were 20 cases in these women, and relative risk adjusted for a number of variables just reached statistical significance, with a relative risk of 2.0, and a 95% confidence interval of 1.03 to 3.4.

Comment

This present research was done to investigate a theory that aspirin might **prevent** pancreatic cancer, as suggested by laboratory experiments and previous small epidemiological study. It found no such thing. The results actually indicate that unless women take relatively large amounts of aspirin (more than 14 tablets a week) for a long time (up to 18 years), there is no significantly increased risk. Even then, what increased risk there is barely achieves statistical significance, with only a few tens of women in this category actually developing pancreatic cancer.

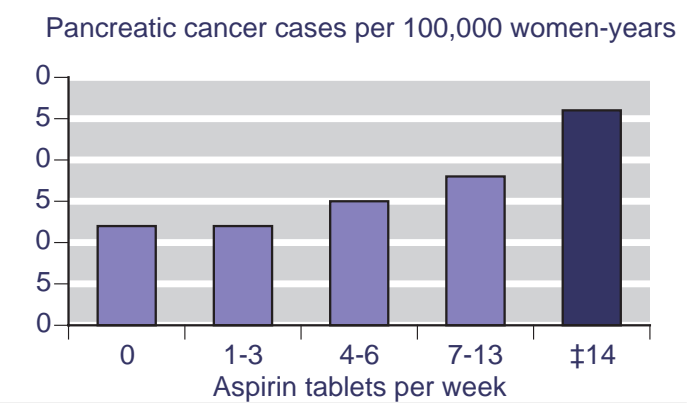
So put the muesli aside and think for a minute. Could this just be a chance finding? Over the 18 years of the study, could a few cases be lost somewhere in the system that might overturn the result? Heavy aspirin users might be taking the aspirin for some reason, and that reason might be linked to pancreatic cancer. What might be called confounding by indication.

There is certainly no evidence here to support a **protective** effect of aspirin. But the evidence that aspirin can cause pancreatic cancer is also weak. It is possible that if 1,000 women took more than 14 aspirin a week for 20 years, pancreatic cancer would develop in two of them, rather than in 1 in 1,000 women who took no aspirin. But unlikely.

Reference:

- 1 ES Schernhammer et al. A prospective study of aspirin use and the risk of pancreatic cancer in women. Journal of the National Cancer Institute 2004 96: 22-28.

Figure 2: Pancreatic cancer according to amount of regular aspirin use: darkest bar is statistically significant



FRACTURE RISK AND SMOKING

We know that smoking is bad for us in many ways, and one of the ways is to decrease bone mineral density. One meta-analysis [1] showed that women who were current smokers were at increased risk for hip fracture. A new analysis [2] extends that analysis to men, to former smokers, and looks at where we live.

Meta-analysis

The new analysis examined PubMed and EMBASE up to mid 2002 for any type of study relating to smoking and fracture that reported relative risk or odds ratio in smokers compared with non-smokers. If subjects had other major diseases they were not included. Smokers were categorised as current smokers (smoking daily), previous smokers (irrespective of when they stopped), and ever smokers, a combination of both.

The outcome was the occurrence of a fracture, with division into any fracture, or hip, wrist, or spine. Analysis was by age, gender and geographical region as well as by smoking status.

Results

Fifty-one studies with 512,000 people were included in the analysis. Current smoking was associated with higher risk of any fracture, and hip and spine fractures, but not wrist fractures. Previous smoking was associated with increased risk only of hip fracture (Table 1). Studies reporting on the amount smoked reported higher risk estimates the more cigarettes smoked. Hip fracture risk was the same in men and women, for current and previous smoking (Table 1).

Latitude was a major influence (Figure 1). Studies in current smokers from northern Europe had a higher risk for hip fractures than those from more southerly latitudes. Studies near the equator had no increased risk, and the risk from southern Europe, the USA and Mexico showed no statistically increased risk (Figure 1).

A clinically important number of fractures may be related to smoking (Table 2). Reducing current smoking would help prevent hip and spine fractures.

Comment

There is much more to this paper than meets the eye. Fascinating was the relationship with latitude, implying that

Table 1: Smoking status and risk of fracture

Fracture site	Smoking status	Relative risk (95%CI)
All sites	Current	1.3 (1.1 to 1.4)
	Previous	1.0 (0.9 to 1.2)
Hip	Current	1.4 (1.2 to 1.6)
	Previous	1.2 (1.1 to 1.4)
Wrist	Current	0.9 (0.5 to 1.6)
	Previous	0.9 (0.7 to 1.1)
Spine	Current	1.8 (1.1 to 2.8)
	Previous	no data
All sites men	Current	1.6 (1.1 to 2.3)
All sites women	Current	1.3 (1.1 to 1.5)
All sites men	Previous	1.4 (1.1 to 1.8)
All sites women	Previous	1.2 (1.1 to 1.4)

exposure to sunlight and vitamin D production might be an important factor.

We should not be surprised by these findings. There is considerable evidence that smoking delays bone repair after fracture or operation, and people undergoing elective orthopaedic surgery would be well advised to stop for that reason alone. Altogether yet another reason to stop smoking and to have another holiday in the sun.

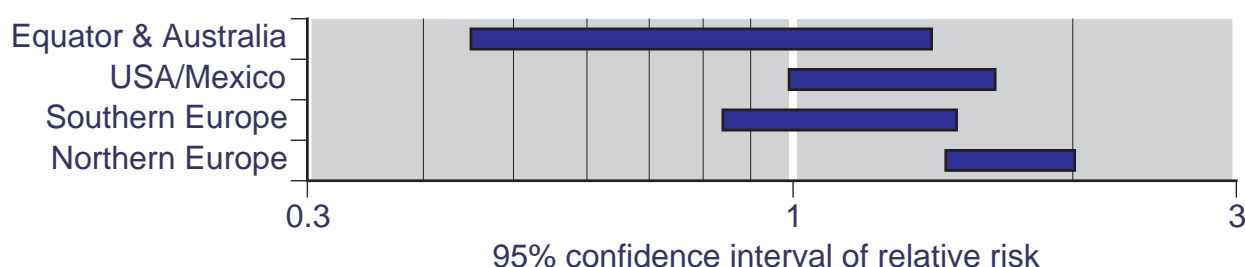
References:

- 1 MR Law, AK Hackshaw. A meta-analysis of cigarette smoking, bone mineral density and risk of hip fracture: recognition of a major effect. *BMJ* 1997 315: 841-846.
- 2 P Vestergaard, L Moskelide. Fracture risk associated with smoking: a meta-analysis. *Journal of Internal Medicine* 2003 254: 572-583.

Table 2: Percentage of fractures attributable to smoking at different levels of smoking in a population

Percentage of current smokers	Percent of fractures attributable to smoking		
	Hip	Spine	All
20	7	13	5
50	16	28	12

Figure 1: Fracture risk and current smoking at different latitudes



BOOK REVIEWS

Stephen Senn. Dicing with death: chance, risk and health. Cambridge University Press, Cambridge. ISBN 0 521 83259 4 (paperback). Pp251. £14.99.

"I am going to try and convince you that when it comes to making decisions and scientific inferences, if you can't count you don't count". That is how Stephen Senn prefaces his book. It is partly about statistics, partly about statisticians, but mostly about thinking and how to think.

While many books on statistics deal with numbers, Senn deals with people. The stars are the men and women who, over the past several hundred years, have developed our understanding of numbers and chance, what today we call statistics. Almost none of them started out as statisticians, but as doctors, chemists, churchmen or some other profession, but who were drawn inexorably to play with numbers as a way of understanding the truth, whatever that is.

For those of us to whom the word Bernoulli means a (now old fashioned) form of computer disk, it is fascinating to learn about the six generations of Swiss Bernoullis, most of whom were shooed away from mathematics but couldn't keep away. Or Poisson of the distribution that actually wasn't his. Or Gene Glass of Nebraska, who credited "Eysenck with the invention of meta-analysis by anti-thesis". Statisticians are people with a particular interest and talent, and we should give thanks to them for helping us understand evidence when we see it.

Equations do not figure a lot, and when they do Senn helpfully tells us when we can afford to skip them. His medium is words, not numbers, and when numbers appear they are as examples to help the flow of the words, rather than obstruct the flow of ideas. A text book this is not. It probably won't help in passing exams, but boy will it help dealing with problems when they come along.

Few readers will walk away and recall the minutiae of arguments about probability. You will understand it when you read it, but five minutes later only the framework will be left. But it is the framework that is the important bit. *Bandolier* despairs at the number of times people fail to realise the lack of importance of trivial chance findings compared with veritable mountains of evidence. MMR is a good example, and the discussion on MMR in the final chapter is great reading.

Senn is urbane, charming, and often funny. He uses quotes a lot, and is not averse to using them against his own values. A favourite is the following: "Meta-analyst: one who thinks that if manure is piled high enough it will smell like roses". Useful for teaching.

So who is this book for? Anyone seeking understanding, teacher or student, professional or public. You might need a dictionary occasionally, but otherwise you can read this in bed or on the beach, and it won't be out of place. *Bandolier* loved it.

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Dylan Evans Placebo. The Belief Effect. Harper Collins London. ISBN 0 00 712612 3 £16.99 pp204

This book is about the placebo effect, the intriguing phenomenon itself and about the underlying mechanism. The structure is first to look at placebos in the context of medical trials, as (negative) controls to help scientists establish the difference between therapeutic effect and a control intervention. The control intervention is there to provide a comparison, and while one might think that a placebo pill or injection should do very little, in fact it can have effect. Evans then proposes a mechanism by which placebo has its effect, and follows with a chapter on the foundation of the belief that triggers physiological events through which placebo might work. The evolutionary context follows, posing questions as to how and why a placebo effect may have evolved. Later chapters focus on alternative medicine and psychotherapy, asking whether they have any greater effect than placebo. Lastly it discusses ethical issues in the context of clinical trials and in clinical practice.

Henry Beecher was, as Evans suggests, the most influential writer on placebo in the mid twentieth century, and the spin on his 1955 paper was that a third of us respond to placebo and the extent of that response was a third of the maximum possible effect. We know now that the proportion of us who respond in any given context varies widely, and that the extent of the response also varies.

These points are vital to the genesis of better clinical trials, and the bottom line is that much of the variation is due to chance, and is minimised by making trials as large as possible. This point does not come through nearly strongly enough. While Evans rightly stresses the importance of statistics in making sense of placebo effects, he often digresses into intriguing results from individual small trials. This is a major hazard of placebo. People have wasted years trying to work out why the placebo effect in a particular trial might be greater in one context than another. Reality is that there is probably a 'true' underlying value for the proportion responding and the extent of the response will only be established with data from many thousands of patients. Individual trials may produce high or low values for placebo response due to chance.

This does not help us determine how placebo has its effect. Evans argues that placebo works by suppressing acute phase responses, our response to injury. He invokes tenuous biochemistry and immunology. Work on whether reversing the body's endogenous opioids, endorphins, with the opioid antagonist naloxone, could reverse the placebo effect has not been satisfactorily replicated. An acute phase response theory is testable, but we may be too simplistic in attempting to discover the (a) mechanism of placebo.

There is also the belief explanation. Beecher tried to categorise placebo responders, who tended to be older, female, believers in authority, and church-attending if not God-believing. Charisma surrounding many alternative therapies and therapists clearly should work to enhance the belief. The consistent failure to show credible therapeutic effect with many of them stands, but it needs to be said that if a therapy makes people feel better that is no bad thing. Just don't badge it as bona fide therapeutic effect. The charisma, the belief, the placebo response, may make you feel better.

Evans defends the legitimacy of placebos in clinical trials in non life threatening conditions to show whether or not treatment is better than placebo. Patients are free to withdraw and have other treatment at any time. It is, after all, unethical to recruit patients into studies that cannot deliver an answer, and without placebo controls that would be the case in many contexts.

Placebo response is intriguing, and this book should bring that interest to a wider audience. There are caveats, but as a one-stop well thought out compilation this is the place to start.